In the Drawings:

A corrected drawing sheet in compliance with 37 CFR 1.121(d), reflecting the sequence identifier for Figure 1, is hereby submitted as a "Replacement Sheet" pursuant to 37 CFR 1.121(d).

REMARKS

Claims 1-15 are pending and stand rejected. Claims 1 and 8 have been amended. Claim 2 has been cancelled. Claims 16-26 have been added. Support for these claims is found throughout the specification, as claim 16 is original claim 1 incorporating the pharmaceutical composition of original claim 13. No new matter has been added. Claims 1, 3-26 are thus now pending.

I. In the Specification:

Applicants have amended the specification on page 1 to provide the priority information requested by the Examiner, specifically that "This application claims foreign priority to EP 02019100.3, filed August 29, 2002".

II. In the Drawings:

Applicants have amended the drawing sheet, labeled as "Replacement Sheet", to reflect sequence identifier for each Figure (Figure 1 corresponds to SEQ ID NO:1) in response to the Examiner's objection and in satisfaction of 37 C.F.R. 1.121(d). Accordingly, Applicants respectfully submit that the objection to the drawings has been obviated.

III. Claim Objection:

Claim 2 stands objected as depending from base claim. Claim 2 has been incorporated into amended Claim 1 and Claim 2 has been cancelled. Applicants submit that Claim 1, as amended, is now in condition for allowance.

Claim 8 stands objected to for missing an article. Applicants have amended Claim 8 to reflect the missing article ("a") as suggested by the Examiner. Accordingly, Applicants respectfully submit that the claim objection to Claim 8 is now obviated and that said Claim 8 is now hereby placed into condition for allowance.

IV. Claim Rejections

A. 35 USC 112, first paragraph

1. Claims 8-15 stand rejected by the Examiner under 35 USC 112, first paragraph for lack of written description. Specifically, the Examiner contends that the claims encompass fragments and alleges that the specification does not demonstrate retention of function for the fragments to demonstrate possession of the genus as claimed in the invention. Applicants respectfully traverse.

Applicants note first of all for the record that the Examiner apparently meant to reject Claims 8-12 only under 35 USC 112, first paragraph. Claims 13-15 reflect pharmaceutical composition(s) dosage/administration amount ranges of the human EPO protein, other components/carrier(s) and a pH amount/range. Claims 13-15 do not recite (or depend on a claim reciting) the "conjugate" terminology which is apparently the basis of the Examiner's rejection. Claims 8-12 do contain the phrase (or depend back to a claim reflecting the phrase) "wherein the erythropoietin protein is a conjugate" and thus these claims seem to be the focus of the Examiner's rejection under 35 USC 112, first paragraph.

With regard to Claims 8-12, Applicants respectfully wish to point out that each claim specifically describes and identifies the analogs claimed, with reference to words, structures and formulae that fully set forth the claimed invention (*Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). In addition, each claim specifically sets forth the limit of said ranges for each of the component parts of the conjugate and its molecular weight and its activity. Support for these claims are found generally throughout Applicants' specification and specifically with regard to paragraphs 23-36 inclusive, and paragraphs 37-52 inclusive demonstrate and describe how to produce said conjugates as claimed. The Examiner acknowledges that the species are adequately described. As the species have included unpegylated and pegylated EPO, epoetin alfa or epoetin beta, 1-6 glycosylation sides and pegylated EPO

with 1-6 glycosylation sides (as depicted in various formula in the specified paragraphs above, as well as methods for making same), Applicant respectfully submits that the genus human EPO has been sufficiently described and disclosed in drawings/structural formula to show Applicant's possession of the claimed genus and thus also, the claimed invention.

2. Claims 13-15 stand rejected under 35 U.S.C. 112, 1st paragraph. The Examiner views the claimed pharmaceutical compositions, without the recitation of a pharmaceutically acceptable carrier or excipient therein, as lacking adequate written description. The Examiner alleges that the composition requires a carrier. Applicants respectfully traverse.

The "essential goal" of the written description requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." In re Barker, 559 F2d 588, 592, n4, 194 USPQ 470, 473, n.4 (CCPA 1577) To satisfy the written description requirement, the applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of the invention. Regents of the University of California v. Eli Lilly, 119 F3rd 1559, 1566, 43 USPQ 2d 1398, 1404 (Fed. Cir. 1997), cert denied, 523 US 1089 (1998).

"There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." MPEP 2163, *In re Wertheim*, 541 F20257, 263, 191 USPQ 90, 97 (CCPA 1976)." The Examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the disclosure a description of the invention as defined by the claims." MPEP 2163.04.

A pharmaceutically acceptable carrier or excipient is conventional in the art and known to those of ordinary skill in the art. Indeed, as noted by the Guidelines for Examination of Patent Applications under 35 USC §112 "Written Description

Requirement", the use of less specific generic language, "such as composition.... does not typically present a written description problem." The Examiner has not provided any reasons why a person skilled in the art at the time the application was filed would not have recognized the description of the limitations in view of the disclosure of the application as filed. (Guidelines, MPEP 2163.04) Indeed, the PTO itself does not require a recitation of a pharmaceutically acceptable carrier or excipient in its classification of certain pharmaceutical composition claims in US Patent Classes 514,772 and 517/769. "The absence of definitions or details for well-established terms" (such as e.g., pharmaceutical composition)" should not be the basis of a rejection under 35 USC 112, para. 1, for lack of adequate written description." (MPEP 2163 Guidelines).

Finally, applicants note that the claimed compositions (as noted below in Applicant's response to the enablement rejection) do describe the conditions and make up of said compositions, including the pH of the composition, the amount of EPO, and at least one other component (sulfate, mannitol, methione, poloxamer) – with each such component and EPO described in ranges or approximations of mass/weight per unit volume. One skilled in the art could readily use these parameters to practice the claimed compositions.

Applicants therefore respectfully submit that its specification and the claimed compositions of claims 13-15 do indeed reasonably convey the invention to one of ordinary skill in the art and that the Examiner has not presented any evidence to the contrary.

B. 35 USC 112, second paragraph

1. Claims 3-15 apparently stand rejected for alleged failure to set forth and claim the subject matter which applicants regard as their invention. The Examiner has rejected claims 3-15 for lack of clear antecedent basis for "the erythropoietin protein" as original claim 1 recites "human erythropoietin".

Applicants have amended Claim 1 to reflect "human erythropoietin protein", thus providing antecedent support to Claims 3-15 and obviating the rejection. Accordingly, Applicants respectfully submit that claims 3-15 are now in condition for allowance.

2. Claims 8 and 11 stand additionally rejected for lack of clear antecedent basis for two reasons: first, the phrase "the erythropoietin protein is a conjugate" as original claim 1 recites "human erythropoietin" and second, the phrase "an erythropoietin protein" as this phrase allegedly reads on more than one protein/fragments which allegedly have no basis in original claim 1.

As noted above, Applicants have amended Claim 1 to reflect "human erythropoietin protein", thus providing antecedent support to Claims 8 and 11 and obviating the first ground of the rejection for these claims.

With regard to the second ground of the rejection, Applicants respectfully posit that both claims refer to an EPO protein which is then modified, this modification makes up the conjugate which is the EPO protein of claim 1. In other words, the EPO protein of claim 1 is in these claims a conjugate, the conjugate comprising an EPO protein + modifications. Accordingly, Applicants respectfully submit that the second ground of rejection to Claims 8 and 11 is inapposite and thus said claims are in condition for allowance.

3. Claims 13-15 stand rejected under 37 USC 112, 2nd paragraph. The Examiner alleges that the recitation of a pharmaceutical composition, without a recitation of a carrier, renders the claims indefinite. Applicants traverse and respectfully reiterate the above 112, first paragraph response here as well. As noted in the MPEP § 2171, whether a claim is indefinite under 112, 2nd paragraph is "evaluated in the context of whether the claim is definite – i.e., whether the scope of the claim is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art." Section 2173 states that "(t)he primary purpose of this requirement of definiteness of claim

language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent." An "applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought. As noted by the court in *In re Swinehart*, 439 F.2d 210, 160 USPQ 226 (CCPA 1971), a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought." (2173.01)

Accordingly, "(i)n reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, "by providing clear warning to others as to what constitutes infringement of the patent". See, e.g, *Solomon v. Kimberly-Clark Corp.*, F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 20000). See also *In re Larsen*, No. 01-1092 (Fed. Cir. May 9, 2001) (unpublished) (The preamble of the *Larsen* claim recited only a hanger and a loop but the body of the claim positively recited a linear member. The court observed that the totality of all the limitations of the claim and their interaction with each other must be considered to ascertain the inventor's contribution to the art. Upon review of the claim in its entirety, the court concluded that the claim at issue apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112 paragraph 2.)."

In the claims at issue, the claimed pharmaceutical compositions comprise and recite a specific range of mass/volume of EPO, and at least one other component in a specified range for each component (in mass or weight/volume) as well as a specified pH range or approximate level. For example, claim 13 recites:

"A pharmaceutical composition for the treatment of disturbances in iron distribution comprising from about 25 to about 2,500 μg/ml of erythropoietin, from about 10 to about 200 mmol/l sulfate and having a pH of from about 6.0 to about 7.0.

Furthermore, there is no necessary prerequisite that a pharmaceutical composition claim has to recite a carrier or excipient. Indeed, Applicants respectfully note that apparently over 6200 patents have been granted containing pharmaceutical composition claims without recitation of a carrier and/or excipient.

The test for definiteness under 35 U.S.C. 112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification. "*Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Applicants respectfully submit that one of ordinary skill in the art would understand the scope of Applicants' pharmaceutical composition claims 13-15.

Accordingly, Applicants respectfully submit that the rejection to claims 13-15 is inappropriate and thus said claims are in condition for allowance.

D. 35 USC 103(a)

Claims 1, 3-12 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Bosman et al. (Diabetes Care, vol. 24, pages 495-499, 2001) in view of HOFFMANN-LA ROCHE (EP 1064 951, January 3, 2001 (cited on IDS – October 3, 2003).

The Examiner contends that Bosman et al. disclose relatedness between erythropoietin deficiency and anemia in patients suffering from early diabetic neuropathy. Specifically the Examiner alleges that the studies in Bosman show anemia associated with EPO deficiency occurs early in insulin dependent diabetes and that one of ordinary skill in the art would conclude that administering EPO to these patients

would result in treatment of their anemia. The Examiner acknowledges that Bosman et al. does not teach erythropoietin with modifications by adding 1 to 6 glycosylation sites, nor does Bosman teach pegylated EPO. However, the Examiner contends that HOFFMANN-LA ROCHE teaches glycosylation of erythropoietin (see page 2 of the reference); and pegylated erythropoietin conjugates and the chemical structures claimed (see claim 4 and 7-15, pages 1-5 of the reference), and that it would have been obvious to one of ordinary skill in the art to combine the teachings of the references. Applicants respectfully traverse.

Pending claims 1 and 3-12 reflect treatment of iron disturbances in patients suffering from non-insulin dependent diabetes mellitus. The Bosman reference apparently only studied anemia in diabetes I patients (insulin dependent) and as such is inapposite to the pending claims. Indeed, applicants note that the Examiner recognized that Bosman did not apply to original claim 2 (new claim 1) as it was not rejected under 103a in the Office Action. As pending claims 3-12 depend directly or indirectly, on now pending Claim 1, Applicants submit said claims are in condition for allowance.

E. The Double Patenting Rejection

Claims 1 and 3-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 3-14 of copending application USSN 10/706,701. As claims 1 and 3-12 of USSN 10/706,701 are not allowed, applicants respectfully submit that this rejection is premature. Applicants request that the double patenting rejection be held in abeyance until there is an indication of allowability of the allegedly overlapping claims in both the instance case and USSN 10/706,701, at which point it can be assessed whether the allowed claims may in fact overlap. Without knowing what subject matter ultimately is allowed in both cases, applicants cannot fairly assess the propriety of the double patenting rejection. Applicants submit that if claims 1, and 3-14 of the instant application as well as certain claims 1 and 3-12 of USSN 10/706,701 are allowed in their current form, Applicants will tender a terminal disclaimer in the latest case that is allowed.

Claims 1 and 3-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 4-15 of copending application USSN 11/013,560. As claims 1 and 4-15 of USSN 11/013,560 are not allowed, applicants respectfully submit that this rejection is premature. Applicants request that the double patenting rejection be held in abeyance until there is an indication of allowability of the allegedly overlapping claims in both the instance case and USSN 11/013,560, at which point it can be assessed whether the allowed claims may in fact overlap. Without knowing what subject matter ultimately is allowed in both cases, applicants cannot fairly assess the propriety of the double patenting rejection. Applicants submit that if claims 1, and 3-14 of the instant application as well as certain claims 1 and 4-15 of USSN 11/013,560 are allowed in their current form, Applicants will tender a terminal disclaimer in the latest case that is allowed if double patenting issues still persist.

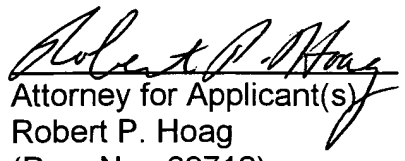
CONCLUSION

The foregoing amendment is fully responsive to the Office Action issued September 1, 2005. Applicants submit that claims 1, 3-15, as amended, are allowable. Applicants respectfully submit that new claims 16-26 are also allowable. Early and favorable consideration is earnestly solicited.

If the Examiner believes there are other issues that can be resolved by telephone interview, or that there are any informalities remaining in the application which may be corrected by Examiner's Amendment, a telephone call to the undersigned attorney is respectfully solicited.

No further fee is required in connection the filing of this Amendment. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,



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